CLINICAL VIGNETTE

Iron Deficiency Anemia Evaluation Reveals a Small Bowel Melanoma

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Case

A 53-year-old Caucasian man originally presented after passing out at work. He had no rectal bleeding or black stools at that time. He had no chest pain or palpitations prior to passing out. He was brought to an outside emergency department and was noted to be anemic with a hemoglobin (Hgb) level of 6.6 g/dL. Iron indices demonstrated iron of 14 ug/dL, iron saturation of 3%, with total iron binding capacity of 503 ug/dL. His stools were positive for occult blood. Subsequent EGD demonstrated a 2 centimeter clean based duodenal bulb ulcer, to which the iron deficiency anemia was attributed (Figure 1). A 2 centimeter hiatal hernia and widely patent schatzki ring were also seen.

The patient was started on omeprazole 20 mg by mouth daily and received two intravenous iron infusions. However, his iron deficiency anemia persisted, with hgb level of 7.6 g/dL and mean corpuscular volume of 71.5 fL three months later. Repeat EGD was performed, which demonstrated healing of the previously noted duodenal bulb ulcer. Colonoscopy was normal. He subsequently underwent a capsule endoscopy that revealed an ulcerated mass in the proximal small bowel (Figure 2).

Single balloon enteroscopy was performed and was not able to identify the mass up to the level of the proximal jejunum. The patient was then referred to a center where double balloon enteroscopy is available. The deeper advancement technique of the double balloon enteroscope revealed a mass in the middle jejunum. The mass was biopsied and a marking tattoo was placed. The biopsy demonstrated malignant melanoma with BRAF V600E positivity. Subsequently a PET CT scan was obtained and revealed two foci of suspicion in the jejunum and ileum, as well as questionable regional lymph nodes. Interestingly, the capsule endoscopy only visualized the proximal lesion; but, it did not pick up the focus in the ileum, despite reaching the colon.

He underwent laparoscopic small bowel resection with anastomosis at both locations and resection of bulky adenopathy. There were no immediate complications. Final pathology demonstrated a 6 centimeter melanoma in the jejunum, involving full thickness of the bowel wall and the subserosal adipose tissue, as well as metastases to zero of three regional lymph nodes. There was also a 4.2 centimeter melanoma in the ileum, involving full thickness of the bowel wall and the subserosal adipose tissue, as well as metastases to two of 22 regional lymph nodes.

Given malignant involvement of two disparate areas within the small bowel, the melanoma was thought to be metastatic from an occult skin lesion rather than a primary small bowel melanoma. Dermatology subsequently evaluated the patient, and skin exam demonstrated no primary skin lesions. Additionally, the patient had no knowledge of prior concerning skin lesions. He is pending planned initiation of the immunotherapy Nivolumab intravenously every two weeks for the next year.

Discussion

Intestinal melanomas can arise as primary tumors, or as metastases from skin, eye or anal melanomas. Most small bowel tumors are likely to be metastases, as less than 2% of small bowel malignant tumors originate as primary tumors in the small bowel. Cutaneous melanoma is one of the most common malignancies to metastasize to the GI tract.[1] In one post-mortem analysis, 43% of patients with malignant melanoma were found to have metastases to the small intestine.[2] Other autopsy studies find that up to 60% of patients who die from melanoma have concurrent metastases to the gastrointestinal tract, but very few are detected prior to death.[1]

Primary and metastatic intestinal melanomas can be difficult to distinguish from one another. This can be a useful distinction to make, as patients with primary melanoma of the small intestine have a worse prognosis than patients with metastases of cutaneous melanoma.[1] According to Sachs et al, a diagnosis of primary intestinal melanoma requires the presence of a solitary intestinal lesion, no metastatic deposits other than those in the regional lymph nodes, and disease free survival of at least 12 months after diagnosis.[3] Often times in cases of small bowel metastatic melanoma, no pre-existing or co-existing primary cutaneous lesion can be identified. The thought is that there may have been spontaneous regression of some prior cutaneous melanoma.[4] For primary or metastatic small bowel melanoma, resection is preferable as the first line therapy. Ideally the resection would have wide margins with complete removal of the lesions. In cases of metastatic disease, the role of surgery is usually for symptomatic relief, as these lesions can cause obstruction, bleeding or profound anemia. Adjuvant therapy is used to improve survival.[1]

With respect to melanoma treatment, Nivolumab is a human IgG4 monoclonal antibody against programmed death 1 (PD-1)

which belongs to the CD28 family and is involved in T-cell regulation. The usual function of PD-1 results in stopping cell death, including death of cancer cells. It is approved as monotherapy for patients with metastatic melanoma. Twelve month recurrence free survival for those with resected stage IV melanoma treated with adjuvant Nivolumab is 63%.[5] Historically, the median survival for metastatic melanoma patients after complete resection was 15 months.[6]

Conclusion

Iron deficiency anemia is one way in which small bowel melanomas can manifest. Even if no primary skin, ocular, or anal melanomas can be detected, metastatic melanoma should be considered when a small bowel melanoma is encountered. The Sachs criteria can be helpful in excluding a primary intestinal melanoma. Emerging therapies like Nivolumab are improving the outcomes in treatment of metastatic melanoma.

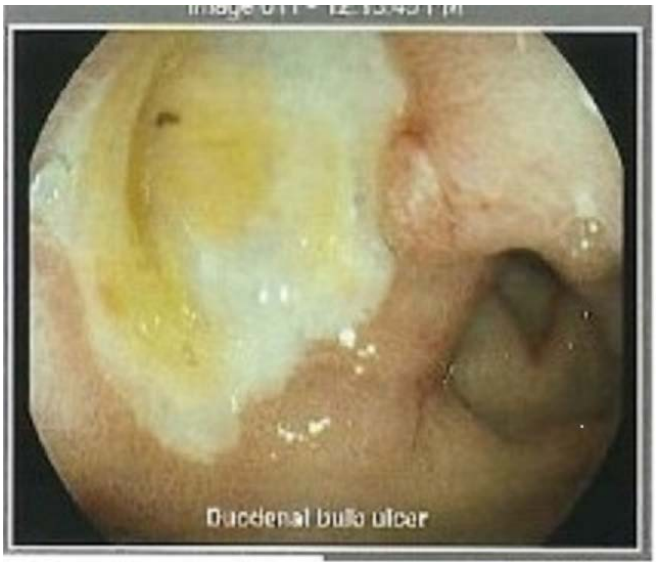

Figure 1.

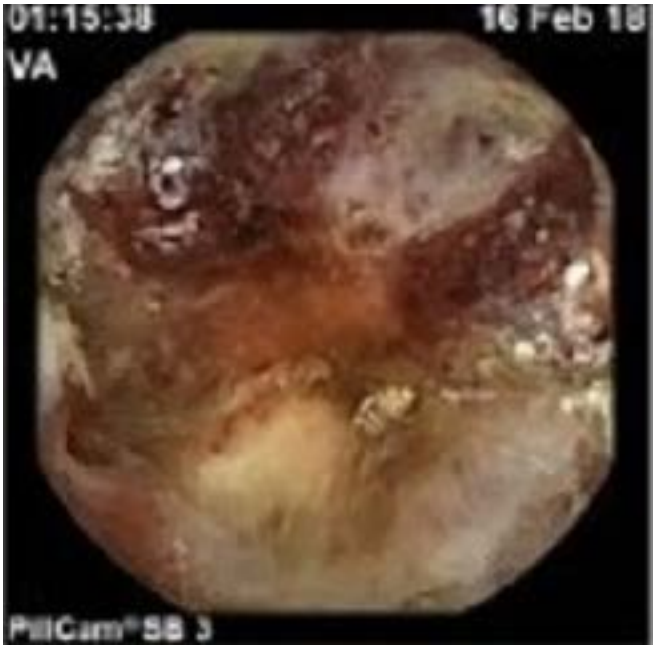

Figure 2.

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